Analysis of the endocardial-to-mesenchymal transformation of heart valve development by collagen gel culture assay.

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Public Summary:
This article describes a method for studying a cellular process, termed endocardial-to-mesenchymal transformation, that is essential for the cardiac progenitor cells to initiate heart valve formation in the developing embryos.

Scientific Abstract:
Malformations of heart valves are one of the most common serious congenital defects. Heart valves are developed from endocardial cushions of the heart. The endocardial cushion in early heart development consists of two cell layers: an outer myocardial cell layer and an inner endocardial cell layer with abundant extracellular matrix (cardiac jelly) in between. Endocardial cells of the cushion, triggered by signals from myocardial cells, delaminate from the surface of the endocardial cushion and undergo transdifferentiation into mesenchymal cells. This process of endocardial-to-mesenchymal transformation (EMT) begins in the atrioventricular canal at embryonic day 9 (E9) and in the cardiac outflow tract at E10 of mouse development. Once formed by the EMT, the mesenchymal cells invade the cardiac jelly, proliferate, and populate the endocardial cushion. The cellularized endocardial cushion then undergoes morphological remodeling; it lengthens and matures into a thin elongated valve leaflet. Here we describe a method to culture endocardial cushions and measure EMT ex vivo. EMT can thus be analyzed independent of other concurrent developmental defects in mice. This culture method also enables ex vivo manipulations of signaling or gene function during EMT to delineate molecular pathways essential for heart valve development.